

WHAT IS CLAIMED IS:

Sub B

1. A method for determining whether a subject has or is predisposed to developing a disease or condition that is associated with an IL-1 inflammatory haplotype, comprising detecting at least one allele of the haplotype, wherein the presence of the allele indicates that the subject is predisposed to the development or has the disease or condition.

2. A method of claim 1, wherein the disease or condition is selected from the group consisting of an inflammatory disease, a degenerative disease an immunological disorder, an infectious disease, a trauma induced disease, and a cancer.

3. A method of claim 1, wherein said detecting step is selected from the group consisting of:

- a) allele specific oligonucleotide hybridization;
- b) size analysis;
- c) sequencing;
- d) hybridization;
- e) 5' nuclease digestion;
- f) single-stranded conformation polymorphism;
- g) allele specific hybridization;
- h) primer specific extension; and
- j) oligonucleotide ligation assay.

4. A method of claim 1, wherein prior to or in conjunction with detection, the nucleic acid sample is subject to an amplification step.

5. A method of claim 4, wherein said amplification step employs a primer selected from the group consisting of any of SEQ ID Nos.8-32.

6. A method of claim 3, wherein said size analysis is preceded by a restriction enzyme digestion.

7. A kit comprising a primer selected from the group consisting of any of SEQ ID NOs. 8-32.

8. A method for selecting an appropriate therapeutic for an individual that has or is predisposed to developing a disease or disorder that is associated with an IL-1 polymorphism, comprising the steps of: detecting whether the subject contains the polymorphism and selecting a therapeutic that compensates for a causative functional mutation that is in linkage disequilibrium with the IL-1 polymorphism.

9. A method of claim 8, wherein said detecting is performed using a technique selected from the group consisting of:

- a) allele specific oligonucleotide hybridization;
- b) size analysis;
- c) sequencing;
- d) hybridization;
- e) 5' nuclease digestion;
- f) single-stranded conformation polymorphism;
- g) allele specific hybridization;
- h) primer specific extension; and
- j) oligonucleotide ligation assay.

10. A method of claim 8, wherein prior to or in conjunction with detecting, the nucleic acid sample is subjected to an amplification step.

11. A method of claim 10, wherein said amplification step employs a primer selected from the group consisting of SEQ ID Nos. 8-32.

12. A method of claim 9, wherein said size analysis is preceded by a restriction enzyme digestion.

13. A method of claim 9, wherein the disease or condition is selected from the group consisting of:

14. A method of claim 9, wherein the therapeutic is a modulator of an IL-1 activity.

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15. A method of ~~claim 14~~, wherein the IL-1 activity is IL-1 $\alpha$ .
16. A method of ~~claim 14~~, wherein the IL-1 activity is IL-1 $\beta$ .
17. A method of ~~claim 14~~, wherein the IL-1 activity is IL-1RN.
18. A method of ~~claim 14~~, wherein the modulator of an IL-1 activity is a protein, peptide, peptidomimetic, small molecule, nucleic acid or a nutraceutical.
19. A method of ~~claim 14~~, wherein the modulator is an agonist.
20. A method of ~~claim 14~~, wherein the modulator is an antagonist.
21. A method for determining the effectiveness of treating a subject that has or is predisposed to developing a disease or condition that is associated with an IL-1 polymorphism with a particular dose of a particular therapeutic, comprising the steps of:
- a) detecting the level, amount or activity of an IL-1 protein; or an IL-1 mRNA or DNA in a sample obtained from a subject;
  - b) administering the particular dose of the particular therapeutic to the subject; detecting the level, amount or activity of an IL-1 protein; or an IL-1 mRNA or DNA in a sample obtained from a subject; and
  - c) comparing the relative level, amount or activity obtained in step a) with the level, amount or activity obtained in step b).
22. A method of ~~claim 21~~, wherein the therapeutic is a modulator of an IL-1 activity.
23. A method of ~~claim 22~~, wherein the IL-1 activity is IL-1 $\alpha$ .
24. A method of ~~claim 22~~, wherein the IL-1 activity is IL-1 $\beta$ .
25. A method of ~~claim 22~~, wherein the IL-1 activity is IL-1RN

26. A method of claim 21, wherein the therapeutic is a protein, peptide, peptidomimetic, small molecule or a nucleic acid.

27. A method of claim 22, wherein the modulator is an agonist.

28. A method of claim 22, wherein the modulator is an antagonist.

29. A method for treating or preventing the development of a disease or condition that is associated with an IL-1 polymorphism in a subject comprising the steps of detecting the presence of at least one IL-1 polymorphism comprising and IL-1 inflammatory haplotype and administering to the subject a therapeutic that compensates for a causative mutation that is in linkage disequilibrium with the at least one IL-1 polymorphism.

30. A method of claim 29, wherein the detecting step is selected from the group consisting of:

- a) allele specific oligonucleotide hybridization;
- b) size analysis;
- c) sequencing;
- d) hybridization;
- e) 5' nuclease digestion;
- f) single-stranded conformation polymorphism;
- g) allele specific hybridization;
- h) primer specific extension; and
- j) oligonucleotide ligation assay.

31. A method of claim 29, wherein prior to or in conjunction with detecting, the nucleic acid sample is subjected to an amplification step.

32. A method of claim 29, wherein said amplification step employs a primer selected from the group consisting of any of SEQ ID Nos. 8-32.

33. A method of claim 30, wherein said size analysis is preceded by a restriction enzyme digestion.

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TO: "DET-STEP"

34. A method of claim 30, wherein the therapeutic is selected from the group consisting of: a modulator of an IL-1 activity.

35. A method of claim 34, wherein the IL-1 activity is IL-1 $\alpha$ .

36. A method of claim 34, wherein the IL-1 activity is IL-1 $\beta$ .

37. A method of claim 34, wherein the IL-1 activity is IL-1Ra.

38. A method of claim 34, wherein the therapeutic is a protein, peptide, peptidomimetic, small molecule or a nucleic acid.

39. A method of claim 34, wherein the modulator is an agonist.

40. A method of claim 34, wherein the modulator is an antagonist.

41. A method for screening for a therapeutic for treating or preventing a disease or condition that is associated with an IL-1 polymorphism comprising a proinflammatory haplotype comprising the steps of:

a) combining an IL-1 polypeptide or bioactive fragment thereof, an IL-1 binding partner and a test compound under conditions wherein, but for the test compound, the IL-1 protein and IL-1 binding partner are able to interact; and

b) detecting the extent to which, in the presence of the test compound, an IL-1 protein/IL-1 binding partner complex is formed, wherein an increase in the amount of complex formed by an agonist in the presence of the compound relative to in the absence of the compound or a decrease in the amount of complex formed by an antagonist in the presence of the compound relative to in the absence of the compound indicates that the compound is an effective therapeutic for treating or preventing the disease or condition.

42. A method of claim 41, wherein the agonist or antagonist is selected from the group consisting of: a protein, peptide, peptidomimetic, small molecule or nucleic acid.

43. A method of ~~claim 42~~, wherein the nucleic acid is selected from the group consisting of: an antisense, ribozyme and triplex nucleic acid.

44. A method of ~~claim 41~~, which additionally comprises the step of preparing a pharmaceutical composition from the compound.

45. A method of ~~claim 41~~, wherein the IL-1 polypeptide is IL-1 $\alpha$ .

46. A method of ~~claim 41~~, wherein the IL-1 polypeptide is IL-1 $\beta$ .

47. A method of ~~claim 41~~, wherein the IL-1 polypeptide is IL-1Ra.

48. A method for identifying a therapeutic for treating or preventing a disease or condition that is associated with an IL-1 polymorphism that comprises an inflammatory haplotype, comprising the steps of:

- a) contacting an appropriate amount of a candidate compound with a cell or cellular extract, which expresses an IL-1 gene; and
- b) determining the resulting protein bioactivity, wherein a decrease of an agonist bioactivity or a decrease in an antagonist bioactivity in the presence of the compound as compared to the bioactivity in the absence of the compound indicates that the candidate is an effective therapeutic.

49. A method of ~~claim 48~~, wherein the modulator is an antagonist of an IL-1 $\alpha$  or an IL-1 $\beta$ , bioactivity.

50. A method of ~~claim 48~~, wherein the modulator is an agonist of an IL-1RN bioactivity.

51. A method of ~~claim 48~~, wherein in step (b), the protein bioactivity is determined by determining the expression level of an IL-1 gene.

52. A method of ~~claim 51~~, wherein the expression level is determined by detecting the amount of mRNA transcribed from an IL-1 gene.

54. A method of claim 51, wherein the expression level is determined using an anti- IL-1 antibody in an immunodetection assay.

56. A method of claim 51, wherein said cell is contained in an animal.

57. A method of claim 56, wherein the animal is transgenic.